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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,575	06/12/2002	Jacques Bartholeyns	0508-1001	1526

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,575	BARTHOLEYNS, JACQUES	
	Examin r	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *02/2002* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1 - 4, filed September 8, 2003 is acknowledged. The traversal is on the grounds that the invention is novel and unobvious, therefore the groups should remain together, that the groups are interconnected, and that the restriction was improper. This is not found persuasive because the inventions of the groups are directed to different inventions which are not connected in design, operation, and/or effect. These inventions are independent since they have different modes of operation, they have different functions, and/or they have different effects. One would not have to practice the various inventions at the same time to practice just one alone. While the search for the groups may be related, it is noted that an overlapping search is not a co-extensive search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5 – 14 are withdrawn as being drawn to non-elected subject matter. Claims 1 – 4 have been examined on the merits.

It is noted:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations f the patentable product**

will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 -- 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and its dependents are drawn to a humanized biomaterial, however are rendered vague and indefinite for reciting "and preferably with macrophages" because a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Moreover, the claims are indefinite because the phrase raises a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims.

Claim 2 is rendered vague and indefinite for reciting "such as aluminum oxide" because a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Moreover, the claim is indefinite because the phrase raises a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims.

Claim 2 is further confusing because it is unclear if applicant intends to include a Markusk group, as the proper language is not used. Applicant may prefer to replace the phrase "chosen among the following materials:" with the phrase "selected from the group consisting of" to more clearly claim the invention.

Claim 2 is rendered vague and indefinite because it is unclear what materials are alternative to the others. Applicant may prefer to use the standard Markush language to more clearly claim the invention. See MPEP 2173.05(h).

In claim 3, line 2, "the human macrophages" lacks sufficient antecedent basis.

Claim 3 is indefinite for reciting "are liable to be" because it is unclear if the macrophages must be obtained as claimed, or merely can be obtained as claimed.

Claim 3 is rendered vague and indefinite for reciting "for instance" because a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Moreover, the claim is indefinite because the phrase raises a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims.

In claim 3, line 9, "patient's" lacks sufficient antecedent basis.

Claim 4 is rendered vague and indefinite for reciting both "comprises" and "consists of" because the transitional phrases are mutually exclusive to one another. It is unclear what applicant intends to include and/or exclude from the claim.

Claim 4 is indefinite for reciting "preferably" because a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Moreover, the claim is indefinite because the phrase raises a question or doubt as to whether the feature introduced by such language is (a) merely

exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1 – 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Naughton et al. (US 4963489 A).

Applicant claims a biomaterial composition comprising a porous biocompatible composite material implanted with monocyte derived cells (macrophages). The biocompatible material is selected from microfibers, ceramic materials, metal oxides, calcium phosphate ceramic, glass fibers, carbon fibers, hydroxylapatite, silicon carbide, silicon nitride, collagen polymers or mixtures thereof; and the macrophages are obtained by ex vivo differentiation of blood monocytes, and are cultured to penetrate and adhere to the biomaterial which are substantially irreversibly bound to the biomaterial (the patient's macrophages). Applicant additionally claims an implant comprising a porous biocompatible composite implanted with monocyte derived cells (macrophages, preferably a scaffold, sponges, bone or cartilage).

Naughton teaches a composite composition comprising a three dimensional support matrix implanted with stromal cells such as monocytes or macrophages (abstract). The composite system is disclosed as a bone or skin implant (col.5 line 33-47). The matrix is made from any material to which cells may attach, and can be woven into a mesh (tissue supporting sponge) (col.7 line 1-12) with collagens (col.9 line 10-17). The cells are autologous (obtained from the patient) and are grown according to the site of implantation (col.7 line 45-51, col.9 line 7-9). (see also col.20 line 10-32, col.21 line 7-13, and col.22 line 5-29).

Although Naughton does not specifically teach the cells are obtained as claimed, the patentability of a product does not depend on its method of production. If the claimed product is the same or obvious from a product in the prior art (i.e. the product disclosed in the cited reference), the claim is unpatentable even though the reference product was made by a different process. When the prior art discloses a product which reasonably appears to be identical with or slightly different than the claimed product-by-process, rejections under 35 U.S.C 102 and/or 35 U.S.C 103 are proper. (MPEP 2113). It is noted that applicant admits that such methods of obtaining macrophages is routine in the art (specification, examples).

Therefore, the reference anticipates the claimed subject matter.

6. Claims 1 – 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al. (US 6139578 A).

Applicant claims a biomaterial composition comprising a porous biocompatible composite material implanted with monocyte derived cells (macrophages). The biocompatible material is selected from microfibers, ceramic materials, metal oxides, calcium phosphate

ceramic, glass fibers, carbon fibers, hydroxylapatite, silicon carbide, silicon nitride, collagen polymers or mixtures thereof; and the macrophages are obtained by ex vivo differentiation of blood monocytes, and are cultured to penetrate and adhere to the biomaterial which are substantially irreversibly bound to the biomaterial (the patient's macrophages). Applicant additionally claims an implant comprising a porous biocompatible composite implanted with monocyte derived cells (macrophages, preferably a scaffold, sponges, bone or cartilage).

Lee teaches a calcium phosphate material seeded with autologous (col.6 line 60-66) living cells (abstract) such as osteoclasts (bone degrading, macrophages) (col.4 line 42-47), used as scaffold implants (col.3-4). Lee additionally teaches autologous implants comprising osteoclast or macrophage cultures on the calcium phosphate material (col.10 line 18-51).

Although Lee does not specifically teach the cells are obtained as claimed, the patentability of a product does not depend on its method of production. If the claimed product is the same or obvious from a product in the prior art (i.e. the product disclosed in the cited reference), the claim is unpatentable even though the reference product was made by a different process. When the prior art discloses a product which reasonably appears to be identical with or slightly different than the claimed product-by-process, rejections under 35 U.S.C 102 and/or 35 U.S.C 103 are proper. (MPEP 2113). It is noted that applicant admits that such methods of obtaining macrophages is routine in the art (specification, examples).

Therefore, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1 – 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton.

Applicant claims a biomaterial composition comprising a porous biocompatible composite material implanted with monocyte derived cells (macrophages). The biocompatible material is selected from microfibers, ceramic materials, metal oxides, calcium phosphate ceramic, glass fibers, carbon fibers, hydroxylapatite, silicon carbide, silicon nitride, collagen polymers or mixtures thereof; and the macrophages are obtained by ex vivo differentiation of blood monocytes, and are cultured to penetrate and adhere to the biomaterial which are substantially irreversibly bound to the biomaterial (the patient's macrophages). Applicant additionally claims an implant comprising a porous biocompatible composite implanted with monocyte derived cells (macrophages, preferably a scaffold, sponges, bone or cartilage).

Naughton teaches a composite composition comprising a three dimensional support matrix implanted with stromal cells such as monocytes or macrophages (abstract). The composite system is disclosed as a bone or skin implant (col.5 line 33-47). The matrix is made from any material to which cells may attach, and can be woven into a mesh (tissue supporting sponge) (col.7 line 1-12) with collagens (col.9 line 10-17). The cells are autologous (obtained from the patient) and are grown according to the site of implantation (col.7 line 45-51, col.9 line 7-9). (see also col.20 line 10-32, col.21 line 7-13, and col.22 line 5-29).

Although Naughton does not specifically teach the cells are obtained as claimed, the patentability of a product does not depend on its method of production. If the claimed product is the same or obvious from a product in the prior art (i.e. the product disclosed in the cited reference), the claim is unpatentable even though the reference product was made by a different process. When the prior art discloses a product which reasonably appears to be identical with or slightly different than the claimed product-by-process, rejections under 35 U.S.C 102 and/or 35 U.S.C 103 are proper. (MPEP 2113). It is noted that applicant admits that such methods of obtaining macrophages is routine in the art (specification, examples).

Naughton does not teach the composite matrix with each of the claimed composite materials or in each of the claimed structures. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to substitute any of the named materials or structures in the implant of Naughton, since they were all well known and used for the same purpose. Moreover, at the time of the claimed invention, one or ordinary skill in the art would have been motivated by routine practice to use any of the claimed implant materials and/or structures in the composite of Naughton with a reasonable expectation for successfully obtaining the composite matrix.

9. Claims 1 – 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee.

Applicant claims a biomaterial composition comprising a porous biocompatible composite material implanted with monocyte derived cells (macrophages). The biocompatible material is selected from microfibers, ceramic materials, metal oxides, calcium phosphate ceramic, glass fibers, carbon fibers, hydroxylapatite, silicon carbide, silicon nitride, collagen

polymers or mixtures thereof; and the macrophages are obtained by ex vivo differentiation of blood monocytes, and are cultured to penetrate and adhere to the biomaterial which are substantially irreversibly bound to the biomaterial (the patient's macrophages). Applicant additionally claims an implant comprising a porous biocompatible composite implanted with monocyte derived cells (macrophages, preferably a scaffold, sponges, bone or cartilage).

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Although Lee does not specifically teach the cells are obtained as claimed, the patentability of a product does not depend on its method of production. If the claimed product is the same or obvious from a product in the prior art (i.e. the product disclosed in the cited reference), the claim is unpatentable even though the reference product was made by a different process. When the prior art discloses a product which reasonably appears to be identical with or slightly different than the claimed product-by-process, rejections under 35 U.S.C 102 and/or 35 U.S.C 103 are proper. (MPEP 2113). It is noted that applicant admits that such methods of obtaining macrophages is routine in the art (specification, examples).

Lee does not teach the composite matrix with each of the claimed composite materials or in each of the claimed structures. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to substitute any of the named materials or structures in the implant of Lee, since they were all well known and used for the same purpose. Moreover, at the time of the claimed invention, one or ordinary skill in the art would have been

motivated by routine practice to use any of the claimed implant materials and/or structures in the implant of Lee with a reasonable expectation for successfully obtaining an autologous implant.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
November 25, 2003.

LEON B. LANKFORD, JR.
PRIMARY EXAMINER